

Remarks:

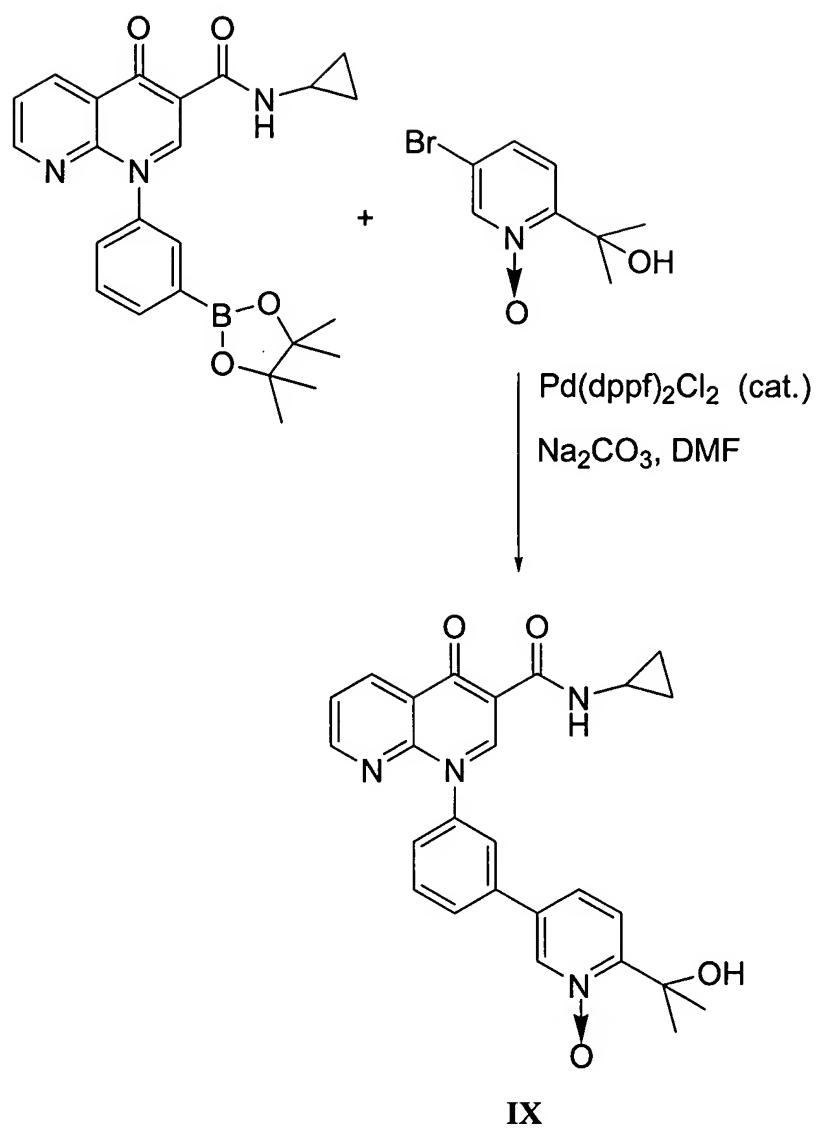
Claims 2 to 6, 10 and 14 to 20 are pending in this application. None of the claims have been allowed.

At the middle of page 2 of the Office Action, the Examiner rejects Claims 1-13 as obvious over Li, et. al., US 6,677,351. The Examiner states:

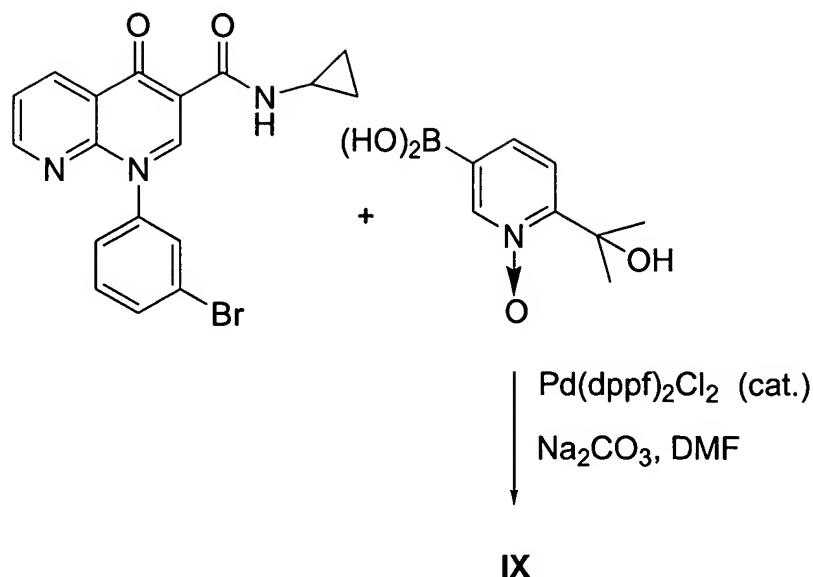
The general synthesis of the same compounds is disclosed in Scheme 2. See col. 23 and 24 where a 1-(leaving group substituted phenyl)naphthyridin-4-one-3-carboxylic acid ester is condensed with a leaving group substituted aryl compound to create a 1-(arylphenyl)naphthyridin-4-one-3-carboxylic acid ester. In the instant case the boronic leaving group is attached to the former while in the reference it is attached to the latter. One of ordinary skill with reference in front of him would find it obvious to do the reverse attachment.

See Ex. 45 at col. 35 and 36 and col. 73 and 74 for the synthesis of the specific compound made in the process of the instant claims.

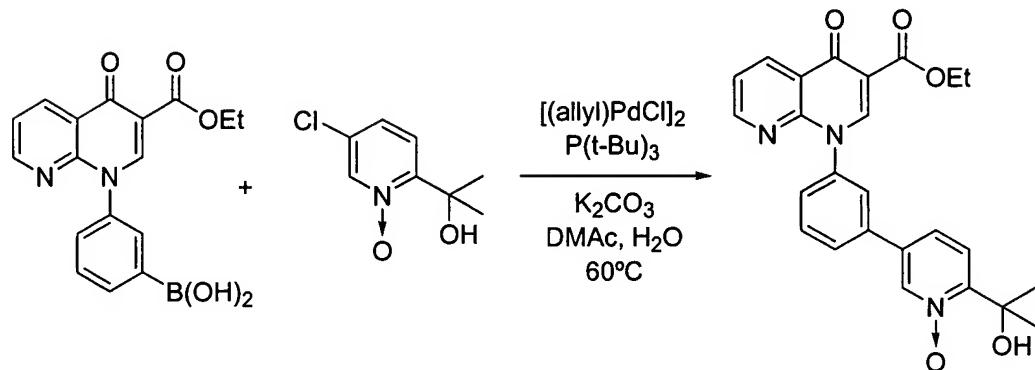
Applicants respectfully traverse. The quoted portion of the Examiner's remarks, suggests that the Examiner may not fully appreciate applicants process and how it differs from the process disclosed in the '351 patent. Drawing from Examples 44 and 45 of the '351 patent, the Examiner's arguments focus on the following step:



The Examiner stated that "In the instant case the boronic leaving group is attached to the former while in the reference it is attached to the latter." It therefore appears that the Examiner to believe that applicants process proceeds as follows:



This is not the case. For example, applicant's exemplified process is as follows:



Thus, assuming, arguendo, one of skill in the art would identify, be motivated by, and adopt the suggestion proposed by the Examiner, he/she would not arrive at applicant's invention. Moreover, applicants respectfully submit that one skilled the art and interested in making large quantities of product, as applicants have, would not follow the teachings and suggestions of the '351 patent.

Applicants note, for example, that the '351 process calls for:

- The use of Palladium in the very last step
- The use of pinacol diborane to make the borone-containing coupling partner
- The cryogenic conditions for making the halo-containing coupling partner

These features are not suitable for large scale production of product intended for humans. Pinacol diborane and use of cryogenic conditions are costly. The use of Palladium catalyst in the last step complicates palladium removal, thereby adding additional process and cost.

As shown above, applicants use a boronic acid. While the boronic ester used in '351 is convenient, it is expensive to prepare. Applicants used a simple boronic acid that is prepared in a one pot synthesis starting from inexpensive 2-chloronicotinoyl chloride. [See the preparation of naphthyridone 7 at page 23 of the instant specification.]

As also shown above, the coupling partner is a chloride rather than a bromide. [Applicants acknowledge that the generic scheme in the '351 patent discloses "XArR²R³" which is described as a halide.] Applicants respectfully submit that their choice is not an obvious one. Applicants' choice allows for the use of an inexpensive starting material (dichloropyridine) and avoids cryogenic conditions of '351 by a selective carbonylation to prepare the coupling partner.

As also shown above, the claimed process installs the cyclopropyl amide of compound IX in the last Step. By distancing the use of palladium from the final step, the palladium can be removed by simple recrystallization of the product. In the '351 patent, palladium is introduced in the final step, and removal of palladium impurities would require column chromatography, or other removal procedures.

Bridging pages 2 and 3 of the Office Action, the Examiner rejects claims 1-13 under 35 USC 112, second paragraph. In particular, the Examiner states that:

Independent claim 1 reacts a step on the way making the N-cyclopropyl-substituted naphthyridine-3-carboxamide product recited therein, but does not recite how the product of said step is converted into said product. The same is true of independent claim 11. Further compound of Formula VIII is recited therein, but its structure is omitted from said claim.

Applicants respectfully submit that the amendments to the claims render the issue moot. Moreover, the amendments to the claims do not present new issues that require the Examiner to conduct a new search. For example, new Claim 14 includes the limitations of Step C, Step D and Step E. Previous Claim 8 was dependent on Claim 7, which in turn was dependent on Claim 1, thereby also including Steps C, D, and E.

Having addressed the outstanding objections and rejections, applicants respectfully submit that their claims are now in condition for allowance and passage thereto is earnestly requested. The Examiner is invited to contact the undersigned attorney at the telephone number provided below, if such would advance the prosecution in this case.

Respectfully submitted,

By *Curtis C. Panzer*
Curtis C. Panzer
Reg. No. 33,752
Attorney for Applicant

MERCK & CO., INC.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-3199